



Thompson, M., Vodicka, T. A., Blair, P. S., Buckley, D. I., Heneghan, C., Hay, A. D. (2013). Duration of symptoms of respiratory tract infections in children: systematic review. *BMJ*, 347, [f7027].  
<https://doi.org/10.1136/bmj.f7027>

Publisher's PDF, also known as Version of record

License (if available):  
CC BY-NC

Link to published version (if available):  
[10.1136/bmj.f7027](https://doi.org/10.1136/bmj.f7027)

[Link to publication record in Explore Bristol Research](#)  
PDF-document

This is the final published version of the article (version of record). It first appeared online via BMJ at <http://www.bmj.com/content/347/bmj.f7027>. Please refer to any applicable terms of use of the publisher.

## **University of Bristol - Explore Bristol Research**

### **General rights**

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:  
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/abr-terms/>

## Appendix 2: Characteristics of included studies [posted as supplied by author]

### A) Trials and observational studies of earache

Study	Study type	Patient population	Inclusion criteria	Exclusion criteria	Outcome(s)	Outcome assessment	Follow-up
<b>Randomised controlled trials</b>							
Burke 1991 (UK)	RCT in 17 general practices of amoxicillin (114) vs. placebo (118) for 7 days	<b>n=118</b> ; ages 3 to 10 yrs, with mean duration of symptoms 30.1 hours before trial entry	<b>Earache</b> and one abnormal eardrum	AB use for AOM during previous week; severe case thought to indicate AB use; allergy to penicillin; enrolled in study during previous year	Mean duration of ear pain, crying, school absences	Parents recorded symptoms in diaries every 4 hours for 24 hours, and then daily for 21 days. Investigator assessed child at home on days 2, 5 to 7, and at clinic on day 8	3 months 96% follow-up (113/118)
Damoiseaux 2000 (The Netherlands)	RCT in 53 general practices of amoxicillin (117) vs. placebo (123) for 10 days	<b>n=123</b> ; ages 6 months to 2 yrs, diagnosed with AOM; 54% had symptoms lasting > 3 days at trial entry	<b>Acute middle ear infection</b> or otorrhoea with fever, recent earache, malaise, and/or irritability	AB use in past 4 weeks; amoxicillin allergy; immunocompromise; craniofacial abnormalities; Down's syndrome; or previous entry into study	% of children with symptoms (day 4); duration of fever (mean), pain/crying (mean)	Parents recorded symptoms in a 10-day diary; clinic visits at days 4 and 11; at 6 weeks, investigator conducted home visits	6 weeks 85% follow-up (105/123)
Hoberman 2011 (USA)	RCT in outpatient hospital clinic and private paediatric clinic of amoxicillin clavulanate (144) vs. placebo (147) for 10 days	<b>n=147</b> ; ages 6 to 23 months, with AOM and at least 2 doses of pneumococcal conjugate vaccine	<b>AOM</b> symptoms (middle ear effusion, bulging or red eardrum and/or pain) lasting less than 2 days; AOM- severity of symptoms score of 3 (range 0 to 14)	Co-occurring infection; chronic illness; symptoms lasting > 2 days; perforated eardrum	% of children with symptoms (days 1 to 7)	Parents recorded AOM severity of symptoms score twice daily for 3 days then once daily, and interviewed daily by telephone until first follow-up visit	21 days 95% follow-up (139/147)
Le Saux 2005 (Canada)	RCT in emergency department of amoxicillin (258) vs. placebo (254) for 10 days	<b>n=246</b> ; ages 6 months to 5 yrs, with symptoms lasting < 4 days	<b>Signs of respiratory tract infection</b> , fever, ear pain, and middle ear effusion (tympanic opacity, impaired mobility, redness or bulging)	AB allergy or use in past 2 weeks; sensitivity to ibuprofen or aspirin; symptoms of mastoiditis or sepsis; otorrhoea; co morbid sinusitis or pneumonia; past middle ear surgery; history of recurrent AOM; immunocompromise; craniofacial abnormalities; chronic or genetic disorder	% of children with symptoms (days 1 to 3)	Parents interviewed by telephone (days 1, 2, 3, 10 to 14); follow-up clinic visits occurred if symptoms persisted or worsened	4 months 91% follow-up (230/254)
Mygind 1981 (Denmark)	RCT in home visit setting of penicillin (72) vs. placebo (77), for 7 days	<b>n=77</b> ; ages 1 to 10 yrs (4.1 yrs, mean), with earache lasting ≤ 24 hours	<b>Ear pain (evidenced by crying) and red or inflamed tympanic membrane</b>	Already receiving treatment for AOM other than aspirin; secretory ear; AB use in past month; suspected chronic otitis media; treatment for secretory otitis media in last year; concurrent disease;	Mean symptom scores (days 1, 3, 5, 7)	Outcomes assessed during follow-up visits in hospital at day 2-3, day 7, 1 month, and 3 months	3 months 73% follow-up (56/77)

penicillin allergy

Neumark 2007 (Sweden)	RCT in 32 health centres of phenoxymethylpenicillin for 5 days (92) vs. no treatment (87)	<b>n=87</b> ; ages 2 to 16 yrs, with unilateral or bilateral AOM lasting < 4 days	<b>Bulging, red eardrum</b> with reduced mobility, diagnosed by pneumatic otoscope or aural microscope	Perforated ear drum; chronic ear conditions; penicillin allergy; current AB use; recurrent AOM; immunocompromise; genetic or mental disorders	Mean symptom duration	Parents recorded symptoms daily in diary for 1 week; nurse conducted telephone interviews at 2 weeks; clinic assessment at 3 months	3 months  Follow-up in control group not reported
Tahtinen 2011 (Finland)	RCT in primary care clinic of amoxicillin clavulanate (162) vs. placebo (160), for 7 days	<b>n=160</b> ; ages 6 to 35 months, with symptoms of respiratory infection and ear pain	<b>Middle ear fluid</b> detected by otoscope; signs of inflammation in tympanic membrane; with fever, ear pain, or respiratory symptoms	Current AB use; perforated eardrum; use of nasal steroids, antihistamines, or oseltamivir in previous 3 days; use of study drugs in last 4 weeks; AB allergy; tympanostomy tubes; severe infection; Down syndrome; immunocompromise; recent vomiting	% of children with symptoms (days 1 to 8)	Parents recorded symptoms in diary; follow-up visits 2 days after enrolment and 1 day after end of treatment. Parents told to call if child's symptoms failed to improve or worsened	8 days  99% follow-up (158/160)
<b>Observational studies</b>							
Greenberg 2003 (Israel)	Prospective observational study in 3 primary care paediatric clinics	<b>n=160</b> ; ages < 3 yrs with acute otitis media	<b>AOM</b> diagnosed by clinician	Diagnosis of AOM $\leq$ 7 days prior to enrolment; immunocompromise or chronic disease; currently receiving acute or chronic medication	Mean duration of illness, sleep disturbance, crying, loss of appetite, fever, day care absence	Telephone interview with parents every 2 to 3 days	21 days  94% follow-up (150/160)
Jedrychowski 2005 (Poland)	1 yr prospective cohort study of pregnant women attending prenatal ambulatory clinic	<b>n=45</b> ; infants' parents reporting ear infection	<b>Ear infection</b> lasting more than 1 day	Not reported	Mean duration of illness	Parent questionnaire administered every 3 months	Until symptom resolution  98% follow-up (333/341 for all symptoms)
Smith 2010 (UK)	Observational cohort study in primary care clinic	<b>n=256</b> ; ages 6 months to 10 yrs, with AOM with (38) or without ear discharge (218)	<b>AOM</b> confirmed by research nurses during home visit $\leq$ 4 hours from initial consultation	Not reported	% with ear pain lasting 1 wk, % with AB use, % with AOM recurrence within 3 months, % of parents reporting hearing problems	Parents recorded symptoms in a diary for 7 days; clinical assessment or follow-up by phone at 2 weeks and 3 months	3 months 100% follow-up of children with ear discharge (38/38)  94% follow-up of children without ear discharge (205/218)

## B) Trials and observational studies of sore throat

Study	Study type	Patient population	Inclusion criteria	Exclusion criteria	Outcome(s)	Outcome assessment	Follow-up
<b>Randomised controlled trials</b>							
Bulloch 2003 (Canada)	RCT in PED of single dose of oral dexamethasone (n=47) vs. placebo (n=52)	<b>n=52</b> ; ages 5 to 16 yrs with GABHS-negative sore throat present <48 hrs before enrolment	<b>Sore throat</b> , painful or difficulty swallowing; erythema of pharynx and symptom onset during previous 48 hours	Varicella exposure; peritonsillar or retropharyngeal abscess; use of corticosteroid in past 2 months; corticosteroid allergy; pregnant; taking AB	Mean times to clinically significant pain resolution & complete pain relief	Parent telephone interview using colour analogue scale with numeric rating guide; verbal description of pain as "mild, moderate or severe"	24 and 48 hrs (or until complete pain relief), and at 1 month  98% follow-up (51/52)
Chapple * 1956 (UK)	RCT in GP of penicillin (n=61) vs. sulphadimidine (n=56) vs. placebo (n=57) for 5 days	<b>n=57</b> ; ages 2 to 10 yrs, with sore throat present < 48 hrs before enrolment (86% of all patients presented with sore throat)	Clinician diagnosis of <b>acute throat</b> or middle ear infection that would have previously resulted in antibiotic provision	Not reported	% of children still unwell at 3 days	Patient or parent assessment at 3 days	3 days  100% follow-up (57/57)
Nelson‡ 1984 (USA)	RCT in paediatric clinic of intramuscular penicillin (n=25) vs. oral placebo for 2 days (n=26)	<b>n=17</b> ; ages 5 to 11 yrs with streptococcal pharyngitis, with sore throat present 24 hrs, median, before enrolment	<b>Presenting with ≥4 fever, sore throat</b> , pharyngeal injection, tonsillar exudate, dysphonia, enlarged, tender anterior cervical lymph node); positive throat culture for GABHS	Cough, rhinorrhea, or penicillin allergy	% of children with duration of sore throat lasting: < 24, 48, > 48 hours; % of children with duration of fever lasting: < 24, 48, > 48 hours	Parents assessed fever at 24, 48, 72 hours; clinician assessment at 2 days	72 hrs  Follow-up unclear; children testing negative for GABHS were excluded from follow-up
Olympia 2005 (USA)	RCT in PED of single oral dose of dexamethasone (n=37) vs. placebo (n=27)	<b>n=27</b> ; ages 5 to 18 yrs with negative test for GABHS; sore throat duration prior to enrolment not reported	<b>Moderate-severe pharyngitis</b> : painful or difficulty swallowing, moderate to severe pharyngeal swelling, and McGrath Facial Affective score of "F" or higher	Immunocompromise, pregnant, allergic to dexamethasone, retropharyngeal or peritonsillar abscess, use of glucocorticoids in previous week	Mean time to complete relief of sore throat	Parent and child assessment using McGrath facial affective scale, reported by daily telephone call	Time until symptom resolution  93% follow-up (25/27)
Ruperto 2011 (Italy)	RCT in 5 paediatric primary care clinics of oral suspension of ketoprofen (33) vs. paracetamol (32) or placebo (32) (all single doses)	<b>n=32</b> ; ages 6 to 12 yrs, with sore throat present less than 1 week	<b>Pharyngotonsillitis</b> , Tonsillo-Pharyngitis score of >5, Children's Sore Throat Pain thermometer score >120	Hypersensitivity or allergy to study medications; use of antipyretic or sore throat lozenge < 6 hours or use of cold medication or analgesic < 8 hours prior to study enrolment	% of children recovered at day 4	Clinician assessment at day 4 visit.	4 days  100% follow-up (32/32)

Zwart 2003 (The Netherlands)	RCT in 43 family practices of 7 days of penicillin (n=46) vs. 3 days of penicillin + 4 days of placebo (n=54) vs. 7 days of placebo (n=56)	<b>n=56</b> ; ages 4 to 15 yrs, with sore throat present mean 3.8 days before enrolment	<b>Sore throat; meeting ≥ 2 Centor criteria</b> (history of fever, absence of cough, swollen lymph nodes, tonsillar exudate)	Complications of respiratory tract infections, AB use, penicillin allergy	Mean duration of sore throat	Parent symptom diary and clinic visit	7 days  76% follow-up (44/56)
<b>Observational studies</b>							
Jedrychowski 2005 (Poland)	1 yr prospective cohort study among pregnant women attending prenatal ambulatory clinic	<b>n=103</b> ; infants' parents reporting sore throat	<b>Sore throat</b> lasting more than 1 day	Not reported	Mean duration of sore throat	Parent questionnaire every 3 months	Until symptom resolution  98% follow-up (333/341 for all symptoms)

### C) Trials and observational studies of cough

Study	Design	Patient population	Inclusion criteria	Exclusion criteria	Outcome(s)	Outcome assessment	Follow-up
<b>Randomised controlled trials</b>							
Bernard 1999 (USA)	RCT in PED and PCP of albuterol (n=30) vs. placebo (n=29) for 7 days	<b>n=29</b> ; ages 1 to 10 yrs; cough present for 1-14 days before enrolment	<b>Cough</b> Lasting 1 to 14 days; respiratory rate ≤ 35 breaths/min	Chronic lung disease, asthma, sinusitis, foreign body, signs of pertussis, current use of prednisolone or bronchodilators, crackles, stridor, pulmonary asymmetry	% of children with persistent cough on days 1 to 7; adverse effects	Cough Impact Score, administered daily by telephone with parent	7 days  79% follow-up (23/29)
Bjornson 2004 (Canada)	RCT in 4 PEDs of single oral dose of dexamethasone (n=359) vs. placebo (n=361)	<b>n=361</b> ; mean age 35 ± 23 months; 30% with history of croup, 13% history of asthma; cough present for mean 0.8 (SD 2.4) days before enrolment	<b>Mild croup</b> Westley croup score ≤ 2 out of 17 and barking cough onset in previous 72 hrs	Signs of other cause of stridor, chronic pulmonary disease, asthma, immunocompromise, varicella exposure in previous 21 days, corticosteroid treatment in previous 2 weeks, epinephrine treatment prior to enrolment	% of children with symptoms (days 1, 2, 3); % returned for care of croup within 7 days; % lost sleep; % parental stress; % adverse events	Telephone Outpatient Score, with parent on days 1 to 3, 7, 21	21 days  96% follow-up (348/361)
Cruz 1995	RCT in ED of single intramuscular dose of	<b>n=19</b> ; ages 6 months to 5 yrs;	<b>Moderate croup or acute laryngotracheitis</b>	Steroid use in previous 24 hrs, structural abnormalities,	Mean duration of illness	Parent telephone interview at 24 hours and at 7 to 10 days,	7 to 10 days

(USA)	dexamethasone (n=19) vs. normal saline (n=19)	cough present for mean 1.04 (SD 1.0) days before enrolment	Westley croup score $\geq 2$ out of 17 with barking cough, hoarseness, or stridor	prior intubation, beta-agonist treatment, epinephrine treatment, or hospitalization needed		using 4 point scale	100% follow-up (19/19)
Geelhoed 1996 (Australia)	RCT in PED of single oral dose of dexamethasone (n=50) vs. placebo (n=50)	<b>n=50</b> ; age > 3 months; 30% with history of croup; cough present for mean 21 (SD 54) hours before enrolment	<b>Mild croup</b> Acute onset of inspiratory stridor, chest wall retractions, barking cough, and hoarseness	Hospital admission for severe croup, use of steroids in last week, pre-existing upper airway condition, history of prolonged stridor, other acute or chronic illness	Mean duration of symptoms; % of children returned for care, or hospitalised	Parent telephone interview once at 7 to 10 days	7 to 10 days  96% follow-up (48/50)
Patel 2003 (Canada)	RCT in PED of albuterol (n=64) vs. placebo (n=65), for 7 days	<b>n=65</b> ; ages < 12 months; cough present for median 4 (IQR 3 to 7) days before enrolment	<b>Bronchiolitis</b> First episode of wheezing; coryza, fever, or cough; well enough to be discharged home.	History of wheezing or home bronchodilator use, premature birth, chronic cardiac or pulmonary disease, immunocompromise, history of immunoprophylaxis therapy	Mean and median durations of illness; time to normal infant and parent sleep patterns; % hospitalised & re-consulting at 2 weeks; trembling; vomiting	4 point scale administered daily over the telephone with parent	2 weeks (or until symptoms resolved)  94% follow-up (61/65)
Plint 2009 (Canada)	RCT in 8 PEDs of nebulised epinephrine + oral dexamethasone (n=200) vs. nebulised epinephrine + oral placebo (n=199) vs. nebulised placebo + oral dexamethasone (n=200) vs. nebulised + oral placebo (n=201); oral treatments given daily for 5 days	<b>n=201</b> ; ages 6 weeks to 12 months; cough present for median 4 (IQR 2 to 6) days before enrolment	<b>Bronchiolitis</b> First episode of wheezing with signs of upper respiratory tract infection during respiratory syncytial virus season. Score of 4 to 15 out of 17 on respiratory distress assessment index	History of bronchodilator use, corticosteroid use in previous 2 weeks, asthma, immunocompromise, history of wheeze, chronic cardiopulmonary disease, premature, varicella exposure in previous 3 weeks, severe respiratory distress	Median duration of symptoms; % admitted to hospital	Standardized telephone interview with parent using 4 point scale, administered daily (days 1 to 7), every 2 days (days 8 to 14), every 3 days (days 15 to 22)	22 days  100% follow-up (201/201)
<b>Observational studies</b>							
Hay 2003 (UK)	Prospective observational study in 8 general practices	<b>n=256</b> ; ages 0-4 yrs; cough present for 5 (3 to 14) days, median (IQR)	<b>Cough</b> Lasting 28 days or less	Asthma or any chronic disease.	Median duration of cough; % re-consulting & hospitalized	Weekly parent interview by telephone. Parents recorded daily symptoms in diary	Until symptom resolution (2 symptom-free days)  89% follow-up (228/256)
Hay 2007 (UK)	Prospective observational study in 13 general practices	<b>n=164</b> ; ages 3 to 59 months; cough present for median 7 days before enrolment	<b>Cough</b> Lasting 28 days or less	Asthma or any chronic disease.	Median duration of cough; % re-consulting & hospitalized	Parent telephone interview. Parents recorded daily symptoms in diary	Until symptom resolution (2 symptom-free days)

							94% follow-up (154/164)
Jedrychowski 2005 (Poland)	1 yr prospective cohort study of pregnant women attending prenatal ambulatory clinic	<b>n=225</b> ; infants' parents reporting cough	<b>Cough</b> Lasting more than 1 day	Not reported	Mean duration of cough	Standardized parent questionnaire administered every 3 months	Until symptom resolution
Kusel 2007 (Australia)	Prospective birth cohort of children in their first 5 yrs of life	<b>n=263</b> ; infants at high-risk of atopy (at least 1 parent with asthma, eczema, or hay fever); data collected from 2,832 episodes	<b>Acute respiratory illness</b> Episodes with runny or blocked nose, cough, "rattly chest" or wheeze (outcome shown only for cough)	Not reported	% of episodes with cough (at 1 to 3 days, 4 to 7 days, 1 to 2 weeks, 2 to 4 weeks); % consulting & % hospitalized	Parent symptom diary and bi- weekly telephone interviews	98% follow-up (333/341 for all symptoms) Until symptom resolution
Petrzella 2010 (USA)	Prospective observational study in PED	<b>n=112</b> ; ages < 12 months old; 21% with history of prematurity; presenting with bronchiolitis	<b>Bronchiolitis</b> First episode of wheezing. Tachypnea, crackles, wheezing, and/or retractions plus history of nasal congestion and/or rhinorrhea	History of bronchodilator use, previous wheezing, bronchiolitis, or asthma, corticosteroid use in last 2 weeks, diagnosis of croup or pneumonia, immunocompromised	Median duration of cough duration, missed days of work and/or day care); % with unplanned medical care	Weekly parent phone interview. Parents recorded daily symptoms in diary	4 weeks or until free of cough for 24 hours
Plint 2004 (Canada)	Prospective observational study in 7 PEDs	<b>n=237</b> ; ages ≤ 12 months; cough present for median 4 days before enrolment, 63% had previously consulted primary care during illness episode	<b>Bronchiolitis</b> First episode of wheezing with signs of upper respiratory tract infection	Not reported	Median symptom duration; % re- consulting & hospitalized	Standardized parent interview by telephone once at 2 to 3 weeks	2-3 weeks 69% follow-up (163/237)

## D) Trials and observational studies of common cold and non-specific respiratory tract infections

Study	Design	Patient population	Inclusion criteria	Exclusion criteria	Outcome(s)	Outcome assessment	Follow-up
<b>Randomised controlled trials</b>							
Hutton 1991 (USA)	RCT in paediatric walk-in clinic and paediatric primary care	<b>n=60</b> ; ages 6 months to 5 yrs, with parent	<b>Common cold</b> Nasal congestion and/or rhinorrhea	Signs of severe illness (fever, vomiting, three loose stools in <24 hours, stridor,	% with improvement in cold symptoms,	Parent interview by telephone at 48 hrs	48 hrs 89% follow-up in

	clinic of antihistamine-decongestant (36) vs. placebo (27) vs. no treatment (33), for 2 days	reporting cold symptoms		wheezing, chest retractions, AB treatment), contraindication to medication	sleeping, appetite, drowsiness, crankiness, vomiting		placebo group (24/27) and 91% in no treatment group (30/33)
Kristo 2005 (Finland)	RCT in primary health centre of cefuroxime (41) vs. placebo (41) for 10 days	<b>n=41</b> ; ages 4 to 10 yrs, with symptoms of acute respiratory infection present mean 8.7 (SD 5.1) days before enrolment	<b>Acute respiratory infection</b> Nasal discharge and obstruction, sneezing, cough, plus abnormal ultrasound of at least one maxillary sinus	Respiratory symptoms lasting > 3 weeks; current AB treatment or use in previous month; allergic to cephalosporin; sinus disease; sinus operation	% with symptom resolution at 2 weeks; % with complications	Parents recorded symptom diary daily. Clinic visit at day 14	2 weeks  90% follow-up (37/41)
Macknin 1998 (USA)	RCT in 2 schools of zinc lozenges (123) vs. placebo lozenges (124), until symptom-free for 6 hours	<b>n=124</b> ; students in grades 1 to 12; 43.9% reporting allergies, 9.2% frequent infections, 14.2% asthma	<b>Common cold</b> ≥ 2 of cough, headache, hoarseness, muscle ache, nasal congestion, nasal drainage, scratchy throat, sore throat, or sneezing	Fever; previous use of zinc; pregnant; adverse reaction to zinc; immunocompromise; other acute illness; symptoms lasting > 24 hours	Median time to symptom resolution	Children recorded symptom score daily in diary; parents' assessment of symptom score was included when it conflicted with child's score	Follow-up until all symptoms resolved  98% follow-up (122/124)
Taylor 2003 (USA)	RCT in 7 private practices, 1 urban clinic, and alternative medicine university of echinacea (263) vs. placebo (261), until symptom resolution (or 10 days maximum)	<b>n=261</b> ; ages 2 to 11 yrs; 207 reporting upper respiratory infection onset in previous 24 hours	<b>Upper respiratory tract infection</b> ≥2 of sneeze, cough, nasal congestion, runny nose, fever	Immunocompromise; asthma, allergic rhinitis, cystic fibrosis, bronchopulmonary dysplasia; allergy to echinacea; taking chronic medications; sibling enrolled in study	Median duration and severity of cold symptoms, fever	Parents recorded symptoms daily in logbook	Follow-up until symptoms resolved (21 days, maximum)  93% follow-up (244/261)
<b>Observational studies</b>							
Butler 2003 (UK)	Prospective observational study among 55 GPs	<b>n=290</b> ; ages 6 months to 12 yrs; presenting with acute upper respiratory infection lasting mean 3.3 (SD 2.18) days at enrolment	<b>Acute upper respiratory infection</b> of suspected viral origin)	AB prescription at initial consultation	Mean duration of illness	Caregiver symptom diary based on Canadian Acute Respiratory Illness and Flu Scale	2 weeks  58% follow-up (169/290)
Carabin 2000 (Canada)	Prospective cohort study in 52 day care centres	<b>n=333</b> ; ages 18 to 36 months; 9.2% with asthma	<b>Upper respiratory tract infection</b> Nasal discharge with fever, cough, sore throat, ear pain, malaise, and/or irritability, preceded by 7 illness-free days	Not reported	Mean & median duration of illness	Parents recorded symptoms on diary and reported data to researchers by telephone biweekly	At least 10 days (over minimum period of 4 weeks)  % participation unknown
Grüber 2007	12 yr prospective birth cohort study in 5 cities	<b>n= 1314</b> ; ages 0 to 7 yrs; 38% at high	<b>Common cold</b> [no further details given]	Not reported	Mean duration of illness	Parents recorded illnesses in symptom diary	Until symptom resolution



(Germany)	(illness duration available only for years 0-7)	risk for atopy					7 yr follow-up not reported
Jacobs 2000 (Canada)	Prospective observational study in primary care clinics in 3 cities	<b>n=220</b> ; ages 0 to 12 yrs; presenting with symptoms lasting < 72 hours	<b>Acute respiratory infection</b> History of fever, with nasal stuffiness, runny nose, cough, or sore throat, and lethargy, myalgia, or headache	Previously consulted for same illness episode; underlying illness requiring daily medication	Median duration of illness until symptoms had receded to ¼ of original score	Parents recorded illnesses in symptom diary using Canadian Acute Respiratory Illness and Flu Scale	2 weeks  94% follow-up (206/220)
Jedrychowski 2005 (Poland)	1 yr prospective cohort study of pregnant women attending prenatal ambulatory clinic	<b>n=292</b> ; infants' parents reporting runny or stuffy nose	<b>Runny or stuffy nose</b> Lasting > 1 day	Not reported	Mean duration of illness	Standardized parent questionnaire administered every 3 months	Until symptom resolution  98% follow-up (333/341 for all symptoms)
Kristo 2006 (Finland)	Prospective cohort study in 2 towns	<b>n=82</b> ; ages 6 to 13 yrs; presenting with acute respiratory infection; Symptoms present average 4 days before recruitment	<b>Respiratory infection</b> , Rhinorrhea and/or cough, lasting < 10 days	AOM or other co-occurring infection requiring AB; upper respiratory infection or AB use in previous 4 weeks; diabetes; immunocompromise; facial anomalies	Mean duration of illness	Parents recorded illnesses in symptom diary	3 weeks  98% follow-up (80/82)
Kusel 2007 (Australia)	Prospective birth cohort of children in their first 5 yrs of life	<b>n=263</b> ; infants at high-risk of atopy (at least 1 parent with asthma, eczema, or hay fever); data collected from 3,526 episodes	<b>Acute respiratory illness</b> Runny or blocked nose, cough, "rattly chest" or wheeze (outcome shown only for runny or blocked nose)	Not reported	% of episodes with runny or blocked nose at 3 days, 4 to 7 days & 2 weeks; % re-consulting; % hospitalized	Parent symptom diary and bi-weekly telephone interviews	Until symptom resolution  90% follow-up (236/263)
Mitra 2011 (UK)	Prospective cohort study of randomly selected children from one region	<b>n=570</b> ; ages 4 to 12 yrs (146 reported illness and are included in analysis)	<b>Acute upper respiratory infection</b> Nasal stuffiness, runny nose, cough or sore throat.	Not reported	Median duration and severity of symptoms	Parents recorded symptoms daily using Canadian Acute Respiratory Illness and Flu Scale daily and returned diary by post once the episode resolved	Until all symptoms resolved (≤ 21 days)  39% follow-up (223/570)
Pappas 2008 (USA)	Prospective cohort study	<b>n=81</b> ; ages 5 to 12 yrs	<b>Common cold</b> Episodes including cough, sneezing, fever, stuffy nose, and/or headache	Not reported	% of children with any symptoms (days 1 to 10)	Parents recorded symptoms on daily diary	10 days  % follow-up unclear
Samet 1993 (USA)	Prospective birth cohort study	<b>n=1,315</b> ; healthy infants	<b>Respiratory illness</b> Episodes lasting ≥ 2 days involving runny or stuffy nose, wet cough, dry	Mother <18 yrs old; non-English speaking mother; mother or household member who smokes;	Median duration of illness	Mothers completed daily symptom diary and reported data to study nurse by telephone biweekly. Nurses	30 days  92% follow-up (1,209/1,315)

			cough, wheeze, or trouble breathing	family plans to move; expectation to attend day care		conducted home visits during illness episodes	
Steinweg 1983 (USA)	Prospective observational study	<b>n=40</b> ; ages 6 months to 5 yrs; presenting with clear or purulent rhinorrhea	<b>Rhinorrhea</b> Previously healthy children with acute onset rhinorrhea not requiring AB treatment	Current or recent AB use; history of >2 ear infections	Mean duration of illness; number of complications	Parents telephoned every 2 days to report symptoms	Until symptoms resolution
Taylor 2010 (USA)	Prospective observational study in 7 paediatric community clinics	<b>N=150</b> ; ages 2 to 11 yrs; 62 with viral upper respiratory infection	<b>Viral upper respiratory infection</b> Runny nose, nasal congestion, cough, and sneezing	History of chronic lung disease; asthma; allergic rhinitis; autoimmune disease; allergy to echinacea	% of children with symptoms (days 1 to 4)	Parents contacted investigators if child developed cold symptoms and recorded symptoms in symptom diaries; parents telephoned every 14 to 17 days to assess progress; children with suspected colds were tested for viral cause	4 day follow-up per cold episode (120 day study period)  99% follow-up (148/150)
Turner Cobb 1998 (UK)	Prospective observational study	<b>n=116</b> ; ages 5 to 16 yrs; 41 had clinically verified upper respiratory infection (35.3%)	<b>Upper respiratory infection</b> Presence of 2 or more specified symptoms for $\geq 24$ hrs, or one symptom for 48 hrs	Families with fewer than 2 children ages 6 to 16 yrs	Mean duration of illness	Children recorded symptoms daily in diary and respiratory episodes were verified by clinical assessment. Symptom diaries were collected every 3 weeks during home visits	15 weeks  % follow-up unclear
von Linstow 2008 (Denmark)	Prospective birth cohort study	<b>n=228</b> ; healthy infants living in close proximity to hospital	<b>Acute respiratory tract illness</b> Nasal discharge with: cough, fever, wheezing, tachypnoea, malaise, and/or lost appetite	Non-Danish or English speaking parents; mothers with serious psychiatric disorders; congenital disease; expectation that family would move within 1 year from enrolment	Mean & median duration of illness	Parents recorded symptoms daily in diaries and were visited monthly to return diaries	1 yr  95% follow-up (217/228)
Wald 1991 (USA)	Prospective birth cohort study of unselected infants born in one hospital	<b>n= 244</b> ; ages 0 to 36 months; ~40% with allergies	<b>Upper respiratory infection</b> Nasal discharge or congestion with or without cough, lasting > 1 day	Congenital disease (e.g. sickle cell anaemia, congenital heart disease, or cystic fibrosis); no access to telephone	Mean duration of illness	Parents interviewed biweekly by telephone by nurse practitioner using a standardized questionnaire	30 to 36 months  63% follow-up (153/244)

Abbreviations: IQR = interquartile range; PCP = Primary care clinic; PED = pediatric emergency department; yr: year; RCT = randomised controlled trial; GP = General Practitioner; AB = antibiotics; AOM = acute otitis media; USA = United States of America; UK = United Kingdom; GABHS = Group A Beta-haemolytic streptococcus